201-14749B

Robust summaries for

Trans-1,2-Dichloroethylene
CAS Number 156-60-5

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Existing Chemical ID: 156-60-5
CAS No. 156-60-5

Producer Related Part
Company: PPG Industries, Inc
Creation date: 25-OCT-2002

Substance Related Part
Company: PPG Industries, Inc
Creation date: 25-OCT-2002

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Reliability (profile): Reliability: without reliability, 1, 2, 3, 4
Flags (profile): Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 Applicant and Company Information

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12-DEC-2002

1.1.0 Substance Identification

IUPAC Name: Ethene, 1,2-dichloro-
Smiles Code: C(=CCL)CL
Mol. Formula: C2H2CL2
Mol. Weight: 96.94

11-DEC-2002

1.1.1 General Substance Information

Purity type: typical for marketed substance
Substance type: organic
Physical status: liquid
Purity: >= 99.7 - % w/w
Colour: clear
Odour: sweetish

11-DEC-2002

1.2 Synonyms and Tradenames

VersaTRANSTM solvent

11-DEC-2002

1.7 Use Pattern

Type: Industrial
Category: Basic industry: basic chemicals

05-DEC-2002

2.1 Melting Point

Value: = -49.4 degree C

Method: other
Year: 1991
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Reliability: (2) valid with restrictions
Data were obtained from the Handbook.
18-AUG-2003 (1)

2.2 Boiling Point

Value: = 48 degree C at 1013 hPa

Method: other
Year: 1985
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Reliability: (2) valid with restrictions
Data obtained from the Handbook.
18-AUG-2003 (2)

2.3 Density

Type: density
Value: = 1.45 g/cm³ at 20 degree C

Method: other
Year: 1991
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Reliability: (2) valid with restrictions
Data obtained from the Handbook.
18-AUG-2003 (1)

2.4 Vapour Pressure

Value: = 353 hPa at 20 degree C

Method: other (measured)
Year: 1991
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: Data obtained from the Handbook. The reference did not describe the detailed method.
Reliability: (2) valid with restrictions
Data obtained from the Handbook.
18-AUG-2003 (1)

2.5 Partition Coefficient

Partition Coeff.: octanol-water
log Pow: = 2.06

Year: 2002
GLP: no

Reliability: (2) valid with restrictions
Data were taken from the collection of data.
06-DEC-2002 (3)

2.6.1 Solubility in different media

Solubility in: Water
Value: = 6300 mg/l at 25 degree C

GLP: no
Test substance: as prescribed by 1.1 - 1.4

Reliability: (2) valid with restrictions
Data were obtained from the handbook.
04-DEC-2002 (1)

3.1.1 Photodegradation

Type: air
Light source: other
DIRECT PHOTOLYSIS
Halflife t1/2: = 3.8 day(s)

Method: other (calculated)
Year: 2002
Test substance: as prescribed by 1.1 - 1.4

Method: The photodegradation half-life is calculated using the EPIWIN/AOPWIN Program. The overall hydroxy radical rate constant is calculated to be 2.8224 E-12 cm3/molecule-sec.
Reliability: (2) valid with restrictions
Data were obtained by modeling.
04-DEC-2002

3.1.2 Stability in Water

Type: abiotic

Year: 2002
Test substance: as prescribed by 1.1 - 1.4

Remark: The information is available at http://toxnet.nil.nih.gov.
Result: Hydrolysis is not expected since chlorinated ethylenes hydrolyze very slowly at environmental conditions.
Reliability: (2) valid with restrictions
Data was obtained from the Hazardous Substance Data Bank's collection of data.
12-DEC-2002

3.3.1 Transport between Environmental Compartments

Type: volatility
Media: water - air
Method: other
Year: 2002
Air: 30.9 **% (Fugacity Model Level I)**
Water: 51.8 **% (Fugacity Model Level I)**
Soil: 17.1 **% (Fugacity Model Level I)**

Method: The EPIWIN is used to perform Level III fugacity modeling. Input to the model were MW (96.94), log Kow (2.06), water solubility (6300 mg/L), MP (-49.44 Degree C), BP (48 Degree C), and VP (264 mmHg). Outputs of the model are the mass percentage, half-life, and emissions in each environmental compartment.
Remark: A mass amount of 0.199% is estimated for sediment using the same model.
Reliability: (2) valid with restrictions
Data were obtained by modeling.
13-AUG-2003

3.5 Biodegradation

Type: aerobic
Concentration: 5 mg/l related to Test substance
10 mg/l related to Test substance
Degradation: = 93 - 95 % after 28 day(s)
Result: other

Method: other
Year: 1981
GLP: no data
Test substance: other TS

Method: The assessments of the biodegradability were conducted using the static-culture flask method.
Result: The test material exhibited moderate biodegradative activity concomitant with the relatively moderate rate of volatilization established in the non-biological volatility control systems. Average total loss of the test material in 28 days total incubation time was 95% with 33% volatilization loss at 5 mg/l level and 93% with 26% volatilization loss at 10 mg/L level.
Test condition: The procedure utilizes biological oxygen demand (BOD) dilution water containing 5 mg of yeast extract per liter, as the synthetic medium; 5 and 10 mg/l concentrations of the test material, a 7-day static incubation of 25 degree C in the dark, followed by three weekly subcultures (totaling 28 days of incubation), and incorporating settled domestic wastewater as microbial inoculum. Gas-chromatographic (GC), the dissolved organic carbon (DOC), and total organic carbon(TOC) analytical procedures were used to determine the extent of biodegradation of the test material. The original culture and three subcultures were included to determine the initial concentration of test material at the beginning of each incubation period. The procedure also incorporated both medium inoculum controls to serve as blank controls for determining baselines for GC analysis, DOC and TOC. Phenol was used as the biodegradable compound to ensure viability of the wastewater inoculum. The biodegradability test was carried out in 250 ml glass-stoppered reagent bottles to minimize possible volatilization of the test material.
Reliability: (2) valid with restrictions
A detailed description of test method and purity of test material were not noted.
26-SEP-2003 (4)

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: static
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no
LC50: = 140 measured/nominal

Method: other
Year: 1978
GLP: no data
Test substance: other TS

Method: This static acute toxicity test followed procedures presented in "Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians" (U.S. EPA 1975).
Result: Measurements of water quality characteristics revealed that dissolved oxygen concentrations of all tests were within a range of 9.7 mg/L at the beginning of an exposure to 0.3 mg/L after 96 h exposure. The pH of the test solutions ranged from 7.9-6.5, and temperature ranged from 21 to 23 Degree C. The 96 hour LC50 was determined to be 140 mg/L with a 95% confidence limit of 120-160 mg/L for **1,2-dichloroethylene**.
Test condition: Test animals utilized were young of the year bluegill obtained from commercial fish suppliers. Upon receipt, each test population was held in a separate tank receiving well water at a minimum flow rate of 4 volume replacement per day. All fish were fed ad libitum daily with dry, pelleted food. All feeding discontinued for 48 hr prior to testing. Test chambers were 19.6 L widemouthed glass jars containing 15 L of test solution. Either a concentrated stock solution was prepared with distilled water or the appropriate amount of the compound was added directly to the diluent in the test jars. Ten fish were randomly selected from a test population and added to each test jar within 30 min after the addition of the test chemical. Dilution water used to prepare the test solutions was deionized water reconstituted according to recommended procedures. The water had a total hardness of 32-48 mg/L CaCO3, a total alkalinity of 28-34 mg/L CaCO3, a pH of 6.7-7.8, a dissolved oxygen concentration of 7.0-8.8 mg/L, a specific conductance as 93-190 umhos/cm. The pH and dissolved oxygen concentration of test solutions were measured at 0, 24, 48, and 96 h of exposure. Fish mortality, behavioral and physiological responses, and solution appearance were observed at time 0 and every 24 hr during exposure. All measurements were made in the control, low, middle, and high test concentrations. The temperature was measured every 24 h in a control jar. The data reported were based on the nominal concentration of the active ingredient.
Test substance: Test chemicals were procured from those commercial sources able to provide the purest grade available. All 64 chemicals tested in this study were >80% pure and test results are

presented as the active ingredient of the formulation. The material tested is 1,2-dichloroethylene. No mention on whether the material is cis- or trans-1,2-dichloroethylene.

Reliability: (2) valid with restrictions
The study meets generally accepted scientific standards and acceptable for assessment.

09-SEP-2003 (5)

Type: static
Species: Lepomis macrochirus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no
LC50: = 74 measured/nominal

Method: other
Year: 1981
GLP: no data
Test substance: other TS

Method: This static acute toxicity test followed procedures presented in "Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians" (U.S. EPA 1975).

Result: Measurements of water quality characteristics revealed that dissolved oxygen concentrations of all tests were within a range of 9.7 mg/L at the beginning of an exposure to 0.3 mg/L after 96 h exposure. The pH of the test solutions ranged from 7.9-6.5, and temperature ranged from 21 to 23 Degree C. The 96 hour LC50 was determined to be 74 mg/L with a 95% confidence limit of 57-91 mg/L for **1,1-dichloroethylene**.

Test condition: Test animals utilized were young of the year bluegill obtained from commercial fish suppliers. Upon receipt, each test population was held in a separate tank receiving well water at a minimum flow rate of 4 volume replacement per day. All fish were fed ad libitum daily with dry, pelleted food. All feeding discontinued for 48 hr prior to testing. Test chambers were 19.6 L widemouthed glass jars containing 15 L of test solution. Either a concentrated stock solution was prepared with distilled water or the appropriate amount of the compound was added directly to the diluent in the test jars. The test jars containing a chemical were capped in an effort to control volatilization. Ten fish were randomly selected from a test population and added to each test jar within 30 min after the addition of the test chemical. Dilution water used to prepare the test solutions was deionized water reconstituted according to recommended procedures. The water had a total hardness of 32-48 mg/L CaCO3, a total alkalinity of 28-34 mg/L CaCO3, a pH of 6.7-7.8, a dissolved oxygen concentration of 7.0-8.8 mg/L, a specific conductance as 93-190 umhos/cm. The pH and dissolved oxygen concentration of test solutions were measured at 0, 24, 48, and 96 h of exposure. Fish mortality, behavioral and physiological responses, and solution appearance were observed at time 0 and every 24 hr during exposure. All measurements were made in the control, low, middle, and high test concentrations.

Temperature was measured every 24 h in a control jar. The data reported were based on the nominal concentration of the active ingredient.

Test substance: Test chemicals were procured from those commercial sources able to provide the purest grade available. All 64 chemicals tested in this study were >80% pure and test results are presented as the active ingredient of the formulation. The material tested is 1,1-dichloroethylene.

Reliability: (2) valid with restrictions
The study meets generally accepted scientific standards and acceptable for assessment.

09-SEP-2003 (5)

4.2 Acute Toxicity to Aquatic Invertebrates

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no
EC50: = 220 measured/nominal

Method: other
Year: 1980
GLP: no data
Test substance: other TS

Method: Procedures used in this acute toxicity test were based on protocols in "Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians (U.S. EPA 1975).

Result: Measurements of water quality characteristics revealed that dissolved oxygen concentrations ranged from 6.5-9.1 mg/L and the range of pH values was 7.4-9.4 units. The 48 hour EC50 value for **trans-1,2-dichloroethylene** was 220 mg/L with a 95% confidence level of 170-290 mg/L.

Test condition: A total of 15 Daphnia magna (<24 hours old) for each level were used for this test. Reconstituted water according to U.S. EPA (1975) with a total hardness of 173 mg/L as CaCO3 and a pH of 8.0 was used. Five to 8 nominal concentrations of test material with a negative control and/or solvent control were tested. The chemicals to be tested was added to 500 ml of diluent water in 2-L jars to prepare each test solution, then the 500 ml volume of test solutions was divided into three, 150 ml aliquots in 250 ml beakers to provide triplicate exposures. Five daphnids were randomly placed in each 150 ml test solutions. For highly volatile chemicals, the tests were conducted in unreplicated 500 ml solutions containing 15 daphnids. These vessels were covered with plastic wrap secured with an elastic band. During this test, the dissolved oxygen concentration, pH and temperature of test solutions were measured at the initiation and termination of the tests in the high, middle, and low test concentrations and controls. Observation of test populations were made at 24 and 48 hours of exposure and any mortalities were recorded.

Test substance: Test chemicals were purchased from commercial chemical suppliers and had a minimum purity of 80%. The chemicals were tested on an active ingredient basis. The material tested is 1,2-dichloroethylene (trans-).
Reliability: (2) valid with restrictions
The study meets generally accepted scientific standards and acceptable for assessment.
26-SEP-2003 (6)

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no
EC50: = 79 measured/nominal

Method: other
Year: 1980
GLP: no data
Test substance: other TS

Method: Procedures used in this acute toxicity test were based on protocols in "Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians (U.S. EPA 1975).
Result: Measurements of water quality characteristics revealed that dissolved oxygen concentrations ranged from 6.5-9.1 mg/L and the range of pH values was 7.4-9.4 units. The 48 hour EC50 value for **1,1-dichloroethylene** was 79 mg/L with a 95% confidence level of 62-110 mg/L.
Test condition: A total of 15 Daphnia magna (<24 hours old) for each level were used for this test. Reconstituted water according to U.S. EPA (1975) with a total hardness of 173 mg/L as CaCO3 and a pH of 8.0 was used. Five to 8 nominal concentrations of test material with a negative control and/or solvent control were tested. The chemicals to be tested was added to 500 ml of diluent water in 2-L jars to prepare each test solution, then the 500 ml volume of test solutions was divided into three, 150 ml aliquots in 250 ml beakers to provide triplicate exposures. Five daphnids were randomly placed in each 150 ml test solutions. For highly volatile chemicals, the tests were conducted in unreplicated 500 ml solutions containing 15 daphnids. These vessels were covered with plastic wrap secured with an elastic band. During this test, the dissolved oxygen concentration, pH and temperature of test solutions were measured at the initiation and termination of the tests in the high, middle, and low test concentrations and controls. Observation of test populations were made at 24 and 48 hours of exposure and any mortalities were recorded.
Test substance: Test chemicals were purchased from commercial chemical suppliers and had a minimum purity of 80%. The chemicals were tested on an active ingredient basis. The material tested is 1,1-dichloroethylene.
Reliability: (2) valid with restrictions
The study meets generally accepted scientific standards and acceptable for assessment.

26-SEP-2003 (6)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Selenastrum capricornutum (Algae)
Endpoint: biomass
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
EC10: measured/nominal
EC50: = 798

Year: 1978
Test substance: as prescribed by 1.1 - 1.4

Method: Data were obtained from EPA's collection of data. No details on test method were provided.
Reliability: (2) valid with restrictions
Data were obtained from EPA's collection of data.
09-SEP-2003 (7)

Species: Skeletonema costatum (Algae)
Endpoint: biomass
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
EC10: measured/nominal
EC50: = 712

Method: other
Year: 1978
Test substance: as prescribed by 1.1 - 1.4

Method: Data were obtained from EPA's collection of data. No details on test method were provided.
Reliability: (2) valid with restrictions
Data were obtained from EPA's collection of data.
09-SEP-2003 (7)

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: mouse
Strain: CD-1
Sex: male/female
No. of Animals: 144
Vehicle: other
Doses: 800-3500 mg/kg bw
Value: = 2122 - 2391 mg/kg bw

Method: other
Year: 1985
GLP: no data
Test substance: other TS

Method: Test method was not noted in the article.
Result: No deaths occurred at doses up to 1200 mg/kg for males and females. The 3500 mg/kg dose was 100% lethal for males and 88% lethal for females. Deaths occurred over a 10 day period following the treatment. Animals dosed at 1600, 2000, and 2400 mg/kg demonstrated signs of decereased activity and ruffled fur within two hours after gavage. In the higher dose groups, there were signs of ataxia, suppressed or total loss of the righting reflex, and ruffled fur. Animals in the 2800 mg/kg groups exhibited ruffled fur for the three days following exposure. Necropsies were performed on all dead animals, and revealed evidence of hyperemia of mucosal surface of the stomach and small intestines. The LD50's with 95% confidence limits were 2122 mg/kg (1874-2382) for male mice and 2391 mg/kg (2055-2788) for female mice.
Test condition: Nine groups (8 per sex) of male and female mice were exposed via an 18 gauge stainless steel stomach tube after 18 hours of fasting. The dosing solutions were prepared in a 1:9 (v/v) solution of emulphor (a polyethoxylated vegetable oil) and deionized water and maintained in the dark at 4 degree C until used. The doses ranged from 800-3500 mg/kg. The mice were observed hourly for the first eight hours for behavioral changes and morbility, then twice therafter for 14 days. All survived mice were necropsied and examined for gross pathology at the end of 14 day test period. LD50 vales were calculated according to the Log Probit procedure.
Test substance: The test material (trans-1,2-dichloroethylene), 98% pure, lot No. LC083187 was obtained from Aldrich Chemical Co., Milwaukee, WI.
Reliability: (2) valid with restrictions
The test method was comparable to Guideline study without detailed description.
18-AUG-2003 (8)

Type: LD50
Species: rat
Strain: Sprague-Dawley
Sex: male/female
No. of Animals: 100
Vehicle: other
Doses: 4500 to 8500 mg/kg bw
Value: = 7902 - 9939 mg/kg bw

Method: other
Year: 1987
GLP: no data
Test substance: other TS

Result: The LD50 and confidence limit for male and female rats were 7902 mg/kg (6805-9175) and 9939 mg/kg (6494-15213), respectively. All deaths occurred within 30 hours after dosing. Central nervous system depression, ataxia, and depressed respiration were observed at all doses; severity was dose-dependent. No treatment related gross necropsy findings were noted.

Test condition: Male and female rats, weighing 113 g and 102 g, respectively, were divided into five groups consisting of 10 rats per sex per group. Animals were fasted overnight before dosing. The test material was administered as a solution in corn oil at a dose volume of 10 ml/kg. Dosages ranged from 450 mg/ml to 850 mg/ml. Hourly observations were made during the first 9 hours after administration of the test material followed by twice daily observations for the next 14 days. All animals that died during the observation period and all survivors were necropsied.

Test substance: The test material (Trans-1,2-Dichloroethylene, Lot No. 5201 J.J.) was obtained from Aldrich Chemical company (Milwaukee, WI). The reported purity was 98%. Identity was confirmed by GC-MS.

Reliability: (2) valid with restrictions
Guideline used and dose levels were not documented. However, all parameters required for the guideline study were evaluated and dose ranges were documented.

26-SEP-2003 (9)

5.1.2 Acute Inhalation Toxicity

Type: LC50
Species: rat
Strain: Sprague-Dawley
Sex: male/female
No. of Animals: 50
Doses: 0, 12300, 22500, 28100, 34100 ppm
Exposure time: 4 hour(s)
Value: = 24100 ppm

Method: OECD Guide-line 403 "Acute Inhalation Toxicity"
Year: 1999
GLP: yes
Test substance: other TS

Method: The study design complied with OECD Guideline for Testing of Chemicals Section 4: Health Effects, No. 403 and U.S. EPA Health Effects Test Guidelines OPPTS 870.1300.

Result: The chamber temperature ranged from 22 to 26 degree C, chamber relative humidity ranged from 32 to 55%, airflow was 37 L/min, and the oxygen concentration was 19-20%. There was no apparent sex difference in the lethality response to the test material and the LC50 for the combined male and female rats was 24100 ppm. All deaths occurred during exposures. One male and three females exposed to 22500 ppm died. Three males and four females exposed to 28100 ppm died. All rats exposed to 34100 ppm died. No rats died at the 12300 ppm exposure group. During exposures, the rats were prostrate, many had their eyes open, and showed a diminished or lack of response to an alerting stimulus. Rats appeared to recover and resume a normal appearance within about 30 minutes after the end of the exposure. Rats exposed to 22500 or 28100 ppm showed lethargy, irregular respiration or weakness immediately after exposure and slight to severe weight loss for one day. There were no effects on gross and microscopic pathology.

Test substance: The test material (Trans-1,2-Dichloroethylene) used for this study was supplied by PPG Industries, Inc. as a clear liquid with a purity of 99.89%.

Test condition: Four groups of 5 male and 5 female rats were exposed whole body to an atmosphere of the test material in air for a single 4-hour exposure period. A control group was exposed similarly except for exposure to the test substance. The test atmosphere was generated by flash evaporating the liquid test substance in nitrogen. The concentration of test material vapor was determined by gas chromatographic analysis. During the 14-day observation period, rats were weighed and observed for clinical signs of toxicity. All rats underwent gross pathologic examination immediately after death or at the end of the 14-day study period and the liver, kidney, heart, and lung were evaluated histopathologically.

Reliability: (1) valid without restriction
26-SEP-2003 (10)

5.1.3 Acute Dermal Toxicity

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5.1.4 Acute Toxicity, other Routes

-

5.4 Repeated Dose Toxicity

Type: Sub-chronic
Species: rat **Sex:** male/female
Strain: Sprague-Dawley
Route of administration: inhalation
Exposure period: 90 days
Frequency of treatment: 6 hours/day, 5 days/week
Post exposure period: one month recovery period
Doses: 0, 200, 1000, or 4000 ppm
Control Group: yes
NOAEL: > 4000 ppm

Method: OECD Guide-line 413 "Subchronic Inhalation Toxicity: 90-day Study"
Year: 1998
GLP: yes
Test substance: other TS

Result: The mean analytically determined concentrations of test substance were as targeted: 200, 1000, and 4000 ppm with standard errors of 0.48, 1.3, and 4.7, respectively. There were no adverse compound-related effects at any concentration level on body weight, clinical observations, body weight gain, food consumption, clinical or anatomical pathology parameters, or liver cell proliferation. The no observed effect level for this study was 4000 ppm, the highest concentration tested in both male and female rats.

Test condition: Four groups of 15 male and 15 female rats each were exposed to analytically determined mean concentrations of 0, 200, 1000, or 4000 ppm and designated for standard toxicity evaluation. Additional four groups of 15 male and 15 female rats each were exposed to the same targeted concentrations of the test substance and designated for cell proliferation evaluation. Rats were exposed whole-body for 6 hours/day, 5 days/week over a 90-day period. Atmospheres containing the test substance were generated by metering liquid material into a heated glass flask with either a pump or a syringe drive. The atmospheric concentration of the test substance was determined by gas chromatography at approximately 15-minute intervals during each exposure. Body weights and food consumption were measured weekly.

Hematology, clinical chemistry, and urine analysis were evaluated in 10 males and 10 females/group after 45 and 90 days. Gross pathologic evaluations were performed on 10 males

and 10 females/group after approximately 90 days and on 5 males and 5 females/group after a 1-month recovery period. The liver, kidneys, lungs, testes, ovaries, adrenal glands, and brain were weighed at necropsy. At the end of exposure period, the standard set of organs were examined microscopically on 10 males and 10 females from the control group and high dose group. Selected organs were evaluated microscopically on 10 males and 10 females from the low and mid exposure groups. Ophthalmological examinations were performed prior to and at the end of the exposure period.

Liver cell proliferation was evaluated in 5 males and 5 females/group after approximately 7, 45, and 90 days. At each time point, rats were implanted with osmotic pumps filled with 20 mg/ml 5-bromo-2-deoxyuridine (BrdU) dissolved in a 0.5 N sodium bicarbonate buffer. Three days after implantation, the rats were sacrificed and the liver and duodenum were processed for immunohistochemical analysis of BrdU incorporation into DNA. The hepatic labeling indices were evaluated for the control and high concentration groups.

Test substance: The test substance (Trans-1,2-Dichloroethylene) was supplied by PPG Industries, Inc. as a colorless liquid with a reported purity of 99.86%. The purity of the test substance was confirmed at the laboratory.

Reliability: (1) valid without restriction

26-SEP-2003 (11)

Type: Sub-chronic
Species: rat **Sex:** male/female
Strain: Fischer 344
Route of administration: oral feed
Exposure period: 14 weeks
Doses: 0, 3125, 6250, 12500, 25000 or 50000 ppm, microencapsulated in feed
Control Group: yes, concurrent no treatment

Method: other
Year: 2002
GLP: yes
Test substance: other TS

Method: The guideline followed for this study was not noted. However, all parameters listed in the OECD/EPA guidelines for a subchronic oral toxicity study were evaluated in this study.

Remark: Microencapsulation allowed continual ingestion of the test substance, was a more appropriate route than oral gavage, and allowed for higher exposure concentrations than would be obtainable in drinking water. Two control groups were included in this study to detect any adverse effects of ingestion of microcapsules.

Result: There were no exposure-related deaths and no clinical findings of toxicity. Results of the FOB indicated no exposure-related findings of neurotoxicity. Mean body weight of male rats in the 50000 ppm group was significantly less than that of the

vehicle controls. Food consumption of the exposed groups was similar to that of the vehicle controls. Exposure concentrations of 3150, 6250, 12500, 25000, and 50000 ppm in the diet resulted in average daily doses of 190, 380, 770, 1540, and 3210 mg/kg for males and 190, 395, 780, 1580, and 3245 mg/kg for females. On day 21 and at week 14, there were mild decreases in hematocrit values, hemoglobin concentration, and erythrocyte counts in the groups of male and female rats at the 25000 and 50000 ppm levels. At week 14, these effects were seen in male rats exposed to 6250 and 12500 ppm. There were no exposure-related alterations in clinical chemistry parameters. The liver weights of female rats exposed to 6250 ppm or greater were significantly greater than those of the vehicle controls. The absolute kidney weights of male rats exposed to 25000 or 50000 ppm were significantly decreased. Sperm motility and vaginal cytology parameters of exposed rats were generally similar to those of the vehicle controls. No gross or microscopic lesions were observed in rats that could be attributed to the test substance exposure.

Very little toxicity was associated with ingestion of the microencapsulated test substance. A maximum tolerated dose was not reached in this study.

Test condition: Groups of 10 male and 10 female rats were fed diets containing 3125, 6250, 12500, 25000 or 50000 ppm microcapsulated test substance for 14 weeks. Microencapsulation was performed by the analytical chemistry laboratory, Midwest Research Institute and the chemical load was determined to be 45%. The dose formulations were prepared at least every 2 weeks by mixing microencapsulated test substance with feed. Clinical findings were recorded weekly. Food consumption was recorded weekly by cage. The animals were weighed initially, weekly, and at the end of the study. A functional observation battery (FOB) was performed on rats in the two control groups and the 12500, 25000, and 50000 ppm groups during weeks 4 and 13. Additional groups of 10 male and 10 female rats received the same exposure concentrations of test substance as the core study animals and were used for clinical pathology testing (on days 5 and 21) only. Hematology and clinical pathology analyses were also conducted on core study rats at the end of the studies. At the end of study, sperm count and motility and vaginal cytology evaluations were conducted on rats in the two control groups and the 12500, 25000, and 50000 ppm groups. Necropsies were performed on all core study animals. The heart, right kidney, liver, lung, right testis, and thymus were weighed. Complete histopathologic examination were performed on rats in the untreated control, vehicle control, and 50000 ppm groups.

Test substance: The test substance (Trans-1,2-Dichloroethylene) was obtained from Aldrich Chemical Company, Inc (Milwaukee, WI) in one lot (MP-0224LP). The study laboratory confirmed that the purity was 99% or greater.

Reliability: (1) valid without restriction
The study is comparable to a guideline study.

26-SEP-2003 (3)

Type: Sub-chronic
Species: mouse **Sex:** male/female
Strain: B6C3F1
Route of administration: oral feed
Exposure period: 14 weeks
Doses: 3125, 6250, 12500, 25000, or 50000 ppm
Control Group: yes, concurrent no treatment

Method: other
Year: 2002
GLP: yes
Test substance: other TS

Method: The guideline followed for this study was not noted. However, all parameters listed in the OECD/EPA guidelines for a subchronic oral toxicity study were evaluated in this study.

Remark: Microencapsulation allowed continual ingestion of the test substance, was a more appropriate route than oral gavage, and allowed for higher exposure concentrations than would be obtainable in drinking water. Two control groups were included in this study to detect any adverse effects of ingestion of microcapsules.

Result: There were no exposure-related deaths and no clinical findings of toxicity. Results of the FOB indicated no exposure-related findings of neurotoxicity. The mean body weights and body weight gains of males and females in the 50000 ppm groups and the body weight gains of females in the 12500 and 25000 ppm groups were significantly less than those of the vehicle controls. Food consumption of the exposed groups was similar to that of the vehicle controls. Exposure concentrations of 3150, 6250, 12500, 25000, and 50000 ppm in the diet resulted in average daily doses of 480, 920, 1900, 3850, and 8065 mg/kg for males and 450, 915, 1830, 3760, and 7925 mg/kg for females. There were no exposure-related alterations in clinical chemistry parameters. The relative liver weights of males exposed to 12500 ppm or greater and females exposed to 25000 or 50000 ppm were significantly greater than those of the vehicle controls. Sperm motility and vaginal cytology parameters of exposed mice were generally similar to those of the vehicle controls. No gross or microscopic lesions were observed in mice that could be attributed to the test substance exposure.

Very little toxicity was associated with ingestion of the microencapsulated test substance. A maximum tolerated dose was not reached in this study.

Test condition: Groups of 10 male and 10 female mice were fed diets containing 3125, 6250, 12500, 25000 or 50000 ppm microcapsulated test substance for 14 weeks. Microencapsulation was performed by the analytical chemistry laboratory, Midwest Research Institute and the chemical load was determined to be 45%. The dose formulation were prepared at least every 2 weeks by

mixing microencapsulated test substance with feed. Clinical findings were recorded weekly. Food consumption was recorded weekly by cage. The animals were weighed initially, weekly, and at the end of the study. A functional observation battery (FOB) was performed on mice in the two control groups and the 12500, or 50000 ppm groups during weeks 4 and 13. Hematology and clinical pathology analyses were also conducted at the end of the studies. At the end of study, sperm count and motility and vaginal cytology evaluations were conducted on mice in the two control groups and the 12500, 25000, and 50000 groups. Necropsies were performed on all animals. The heart, right kidney, liver, lung, right testis, and thymus were weighed. Complete histopathologic examination were performed on mice in the untreated control, vehicle control, and 50000 ppm groups.

Test substance: The test substance (Trans-1,2-Dichloroethylene) was obtained from Aldrich Chemical Company, Inc (Milwaukee, WI) in one lot (MP-0224LP). The study laboratory confirmed that the purity was 99% or greater.

Reliability: (1) valid without restriction
The study is comparable to a guideline study.

26-SEP-2003 (3)

Type: Sub-chronic
Species: rat **Sex:** male/female
Strain: Sprague-Dawley
Route of administration: drinking water
Exposure period: 90 days
Doses: 0, 500, 1500, and 3000 mg/kg
Control Group: yes
NOAEL: > 3000 mg/kg

Method: other
Year: 1987
GLP: no data
Test substance: other TS

Method: The guideline followed for this study was not noted. However, all parameters listed in the OECD/EPA gruidelines for a subchronic oral toxicity study were evaluated in this study.

Result: Exposure for 90 days to theoretical daily doses of 500, 1500, or 3000 mg/kg/day failed to elicit significant compound-related and dose-dependent adverse effects on body weight, general behavior, hematology, urinalysis, or serum chemistries. There were compound-related and dose-dependent increases in kidney weights and ratios in treated female rats. However, there were no histopathologically apparent lesions.

The actual daily doses were 402, 1314, and 3114 mg/kg for males and 353, 1257, and 2809 mg/kg for females.

Test condition: Trans-1,2-dichloroethylene was administered in drinking water solution to five groups consisting of 20 male and 20 female rats. The groups were naive untreated control, 1% emulphor vehicle control, 500 mg/kg, 1500 mg/kg, and 3000 mg/kg. Water solutions were prepared twice weekly by the addition of test

substance to 1% emulphor (GAF Corp., Linden, NJ) in deionized water.

Rats were examined twice daily for general appearance, signs of intoxication, and death. Body weights were recorded on the first day of exposure, weekly thereafter, and at death. Consumption of drinking water solutions were determined twice weekly. Hematology, blood chemistry determinations, and urinalyses were conducted at the end of the 90-day exposure period. At the end of exposure period, a gross pathological examinations were performed and selected organs were weighed. Liver, kidneys, testes, and ovaries were examined histologically. The data were subjected to an analysis of variance, Dunnett's t-test, and a test of homogenicity. Nonhomogeneous data were subjected to a Wilcoxon rank sum test. Those values that differed from the vehicle control group at $p<0.05$ were considered statistically significant.

Test substance: The test substance (Trans-1,2-Dichloroethylene) was obtained from Aldrich Chemical Company (Milwaukee, WI). The reported purity was 98%. Identity was confirmed by GC-MS.

Conclusion: The toxicity from exposure to trans-1,2-dichloroethylene in drinking water apparently is low and probably does not constitute a serious health hazard.

Reliability: (1) valid without restriction
The study is comparable to a guideline study.

18-AUG-2003 (9)

Type: Sub-chronic
Species: mouse **Sex:** male/female
Strain: CD-1
Route of administration: drinking water
Exposure period: 90 days
Doses: 0.1, 1.0, 2.0 mg/ml
Control Group: yes, concurrent no treatment

Method: other
Year: 1985
GLP: no data
Test substance: other TS

Method: The guideline followed for this study was not noted.

Result: The average doses of the test substance consumed on a mg/kg/day basis over the 90 day period were 17, 175, and 387 for the males and 23, 224, and 452 for the females. Few adverse effects were observed in either sex following 90 days of exposure. The most noteworthy changes occurred in the males exposed to the highest level of test substance, where there was a significant decrease in glutathione levels, and in the females exposed to all three levels of the test substance, where there was a significant decrease in aniline hydroxylase activity. No changes were observed in the cell-mediated immune status of either sex or in the humoral immune status of females. However, a marked suppression in humoral immune status was observed in male mice exposed to all three levels

of test substance, as indicated by a decreased ability of spleen cells to produce antibody against sheep erythrocytes (sRBC). Macrophage function was depressed only in females, as indicated by the decreased ability of thioglycollate-recruited peritoneal exudate cells (PEC) to phagocytize sRBC.

Test condition: Trans-1,2-dichloroethylene was administered in the drinking water dissolved in deionized water containing 1% emulphor at either 0.1, 1.0, or 2.0 mg/ml. These concentrations were calculated to deliver approximately 1/100, 1/10, and 1/5 the LD50. In addition, a group receiving deionized water served as controls. There were 260 mice of each sex in the control group and 140 mice of each sex in each treatment group. These animals were divided into subsets of animals that were evaluated for various standard toxicological endpoints and various immunologic endpoints. The standard toxicological assessments included fluid consumption, body and organ weights, hematology, serum and liver chemistries, necropsy, hepatic microsomal activities, and blood coagulation. Bone marrow status was evaluated by assessing DNA synthesis. Humoral immunity was evaluated by determining the number of IgM Spleen antibody-forming cells (AFC) to sheep erythrocytes (sRBC), the serum antibody level to sRBC, and spleen lymphocyte response to the B cell mitogen, lipopolysaccharide (LPS). The status of cell-mediated immunity was assessed by quantitating the delayed type hypersensitivity (DTH) response to sRBC, proliferation of the popliteal lymph node, and the spleen cell response to the T lymphocyte mitogen, Concanavalin A (Con A). Macrophage function was evaluated by measurement of the vascular clearance rate and distribution of radiolabeled sRBC in the liver, spleen, lungs, and thymus, and the recruitability, adherence, chemotaxis, and phagocytic activity of peritoneal exudate cells (PEC).

Test substance: The test substance (Trans-1,2-Dichloroethylene), 98% pure, Lot No. LC083187, was obtained from Aldrich Chemical co., Milwaukee, WI.

Conclusion: The most notable effects of oral exposure to DCE were decreased glutathione levels in males and decreased aniline hydroxylase activity in females. The immune system of random-bred CD-1 mice does not appear to be overly sensitive to the effects of test substance. The few effects which were seen were probably the result of general toxicity as opposed to specific target organ toxicity.

Reliability: (2) valid with restrictions
The study is comparable to a guideline study with an exception. A microscopic evaluation was not conducted.

26-SEP-2003 (12)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: TA98, TA100, TA1535, and TA1537
Concentration: 0, 33.3, 100, 333.3, 1000, 3333.3, 10000 ug/plate
Cytotoxic Concentration: 10000 ug/plate
Metabolic activation: with and without
Result: negative

Method: other
Year: 1986
GLP: no data
Test substance: other TS

Result: The test material was not mutagenic in any of four strains of S. typhimurium with or without induced hamster or rat S9 metabolic activation enzymes.

Test condition: The test substance was tested and evaluated in the preincubation assay as a coded sample using Salmonella strains TA1535, TA1537, TA98, and TA100 with and without Aroclor 1254-induced rat and hamster metabolic activation systems. The metabolic activation system, S-9 mix were prepared from male Sprague-Dawley rats and male Syrian hamsters that had been induced by an i.p. injection of Aroclor 1254 (500 mg/kg) five days before sacrifice. 0.5 ml of S-9 mix or 0.1M PO4 buffer (pH 7.4), 0.05 ml of the overnight culture, and 0.05 ml of solvent or chemical dilution were added to test tubes maintained at 37 degree C. The mixture was mixed and incubated at 37 degree C for 20 min., at which time 2.5 ml of molten top agar supplemented with 0.5 mM L-histidine and 0.5 mM D-biotin were added. The contents of the tubes were mixed and poured onto 25 ml of minimal glucose bottom agar and incubated at 37 degree C for 48 hr. Each trial consisted of triplicate plates of concurrent positive and negative controls and five doses of the test substance with and without metabolic activation. The trial was repeated after completion of the first trial. The numbers of revertant colonies from each set of 3 plates were averaged and the standard error was calculated. The positive controls in the absence of metabolic activation were sodium azide (TA 100 and TA 1535), 9-aminoacridine (TA 1537), and 4-nitro-o-phenylenediamine (TA 98). The positive control for metabolic activation with all strains was 2-aminoanthracene. The test material was considered a mutagen if a dose related, reproducible increase in the number of revertants over background, even if the increase was less than twofold.

Test substance: The test substance (Trans-1,2-Dichloroethylene) was obtained from Aldrich Chemical Company, Inc (Milwaukee, WI) and the purity was reported as 98%.

Reliability: (1) valid without restriction
Even though a specific guideline number was not mentioned in the reference, the procedure included all parameters required for the guideline.

13-AUG-2003 (13)

Type: Cytogenetic assay
System of testing: Chinese hamster ovary (CHO) cells
Concentration: 160 - 5000 ug/ml for SCE, 1600 - 5000 ug/ml for CA
Metabolic activation: with and without
Result: negative

Method: other
Year: 1987
GLP: no data
Test substance: other TS

Result: The test material did not induce Sister Chromatid Exchanges (SCEs) without S9; the results of a single trial with S9 were judged to be equivocal based on the trend test (P<0.005) and the absence of significant increases (>20%) at any of the individual dose points.

No induction of chromosomal aberrations observed in cultured CHO cells with or without S9.

Test condition: The test substance was tested in cultured Chinese hamster ovary (CHO) cells for induction of sister chromatid exchange (SCEs) and chromosomal aberrations (Abs), both in the presence and absence of Aroclor 1254 induced male Sprague-Dawley rat liver S9 and cofactor mix. Each test consisted of concurent solvent and positive controls and of three to four doses of the test substance. A single flask per dose was used. The positive control was cyclophosphamide.

SCE test: Dose levels used for this test were 160, 500, 1600, or 5000 ug/ml. In the test without S9, CHO cells were incubated for 26 hours with the test substance in supplemented McCoy's 5A medium. Bromodeoxyuridine (BrdU) was added 2 hours after culture initiation. After 26 hours, the medium containing the test substance was replaced with fresh medium plus BrdU and Colcemid, and incubation was continued for 2 hours. Cells were then harvested, fixed, and stained with Hoechst 33258 and Giemsa. In the test with S9, cells were incubated with test substance, serum-free medium, and S9 for 2 hours. The medium was then replaced with medium containing serum and BrdU and no test material. Incubation proceeded for an additional 26.5 hours with Colcemid present for the final 2 hours. Harvesting and staining were the same as for cells treated without S9. Fifty second-division metaphase cells were scored for frequency of SCEs/cell from each dose level. Statistical analyses were conducted on the slopes of the dose-response curves and the individual dose points. An increase of 20% or greater at any single dose was considered weak evidence of activity; increases at two or more doses resulted in a positive assay.

Chromosomal Aberration Test: Dose levels used for the test were 1600, 3000, or 5000 ug/ml. In the test without S9, cells were incubated in McCoy's 5A medium with the test material for 10 hours. Colcemid was added and incubation continued for 2

hours. The cells were then harvested, fixed, and stained with Giemsa. For the test with S9, cells were treated with test material and S9 for 2 hours, after which the teatment medium was removed and the cells were incubated for 11 hours in fresh medium, with Colcemid present for the final 2 hours. Cells were harvested in the same manner as for the treatment without S9. Two hundred first division metaphase cells were scored at each dose level. Classes of aberrations included simple (breaks and terminal deletions), complex (rearrangements and translocation) and other (pulverized cells, despiralized chromosomes, and cells containing 10 or more aberrations). Chromosomal aberration data are presented as % of cells with aberrations. Statistical analyses were conducted on both the dose response curve and individual dose points. A statistically significant differences for one dose point and a significant trend was considered weak evidence for a positive response; significant differences for two or more doses indicated the trial was positive.

Test substance: The test substance (Trans-1,2-Dichloroethylene) was obtained from Aldrich Chemical Company, Inc (Milwaukee, WI) and the purity was reported as 98%.

Reliability: (1) valid without restriction
Even though a specific guideline number was not mentioned in the reference, the procedure included all parameters required for the guideline.

26-SEP-2003 (3)

5.6 Genetic Toxicity 'in Vivo'

Type: Cytogenetic assay
Species: mouse **Sex:** male
Strain: B6C3F1
Route of admin.: i.p.
Doses: 500, 1000, 2000 mg/kg
Result: negative

Method: other
Year: 2002
GLP: no data
Test substance: other TS

Result: The test substance administered by i.p. injection at doses of 500 to 2000 mg/kg induced no SCEs or Abs in bone marrow cells of male mice.

Test condition: Sister Chromatid Exchange Test: Male mice (five animals per dose group) were injected intraperitoneally with the test substance dissolved in corn oil. Vehicle control animals received an equivalent injection of corn oil only. The positive control was dimethylbenzanthracene. A standard harvest time of 23 hours was used. The animals were implanted subcutaneously with a BrdU tablet 24 hours before harvest (1 hour before the treatment). Two hours before sacrifice, the animals received an i.p. injection of colchicine in saline.

The animals were killed 23 hours after treatment (24 hours after BrdU dosing). One or both femurs were removed, and the marrow was flushed out with phosphate-buffered saline (pH 7.0). The cells were treated with a hypotonic salt solution, fixed, and dropped onto chilled slides. The slides were stained with fluorescence-plus-Giemsa and scored. Twenty-five second metaphase cells were scored from each of four animals per treatment group. Responses were evaluated as SCEs/cell and the data were analyzed by a trend test.

Chromosomal Aberration Test: Male mice (10 animals per dose group) were injected i.p. with the test substance dissolved in corn oil. Vehicle control group received equivalent injections of corn oil only. The positive control was dimethylbenzanthracene. The animals were subcutaneously implanted with a BrdU tablet 18 hours before the scheduled harvest. Two hours before sacrifice, the animals received an i.p. injection of colchicine in saline. The animals were killed 17 hours after the test substance injection. One or both femurs were removed, and the marrow was flushed out with phosphate-buffered saline (pH 7.0). Cells were treated with a hypotonic salt solution, fixed, and dropped onto chilled slides. The slides were stained with fluorescence-Giemsa and scored. Fifty first division metaphase cells were scored from each of seven or eight animals per treatment group. Responses were evaluated as the percentage of aberrant metaphase cells, excluding gaps. The data were analyzed by a trend test.

Test substance: The test substance (Trans-1,2-Dichloroethylene) was obtained from Aldrich Chemical Company, Inc (Milwaukee, WI) and the purity was reported as 98%.

Reliability: (1) valid without restriction
Even though a specific guideline number was not mentioned in the reference, the procedure included all parameters required for the guideline.

18-AUG-2003 (3)

Type: Micronucleus assay
Species: mouse **Sex:** male/female
Strain: B6C3F1
Route of admin.: oral feed
Exposure period: 14 weeks
Doses: 0, 3125, 6250, 12500, 25000 or 50000 ppm, microencapsulated in feed
Result: negative

Method: other
Year: 2002
GLP: no data
Test substance: other TS

Result: The test substance administered in microcapsules in feed for 14 weeks did not increase the frequency of micronucleated normochromatic erythrocytes (NCEs) in the peripheral blood of male and female mice. In addition, no effect on the

percentage of micronucleated polychromatic erythrocytes among the total erythrocyte population was observed, indicating no inhibition or stimulation of erythropoiesis in the bone marrow of exposed mice.

Test condition: At the end of the 14-week toxicity study (see section 5.4 for details), peripheral blood samples were obtained from male and female mice. Smears were immediately prepared and fixed in absolute methanol. The methanol-fixed slides were stained with acridine orange and coded. Slides were scanned to determine the frequency of micronuclei in 2000 normochromatic erythrocytes (NCEs) in each of 10 animals per exposure group. In addition, 1000 polychromatic erythrocytes (PCEs) were scored per animal to determine the percentage of PCEs in the total erythrocyte population. The frequency of micronucleated cells amoung NCEs was analyzed by a statistical software package that tested for increasing trend over exposure groups with a one-tailed Cochran-Amitage trend test, followed by pairwise comparisons between each exposure group and the untreated control group. An individual trial is considered positive if the trend test P value is less than or equal to 0.025 or if the P value for any single exposed group is less than or equal to 0.025 divided by the number of exposed groups.

Test substance: The test substance (Trans-1,2-Dichloroethylene) was obtained from Aldrich Chemical Company, Inc (Milwaukee, WI) and the purity was reported as 98%.

Reliability: (1) valid without restriction
Even though a specific guideline number was not mentioned in the reference, the procedure included all parameters required for the guideline.

26-SEP-2003 (3)

5.8.1 Toxicity to Fertility

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5.8.2 Developmental Toxicity/Teratogenicity

Species: rat **Sex:** female
Strain: Crj: CD(SD)
Route of administration: inhalation
Exposure period: Days 7-16 of gestation
Frequency of treatment: 6 hours per day
Duration of test: Days 7-16 of gestation
Doses: 2000, 6000, 12000 ppm
Control Group: yes, concurrent no treatment
NOAEL Maternal Toxity: < 2000 ppm
NOAEL Teratogenicity: = 6000 ppm

Method: EPA OTS 798.4350
Year: 1988
GLP: yes
Test substance: other TS

Remark: Significant increases in the mean number of resorptions per litter were seen in the litters of dams exposed to 6000 and 12000 ppm of test substance; however, these values are within the range of historical controls and not considered to be exposure related.

Result: The mean daily chamber concentrations were within 5% of the desired concentrations throughout the exposure period. Overt maternal toxicity was observed as a significant reduction in weight gain at 12000 ppm and in feed consumption at 6000 and 12000 ppm. A significant body weight gain supression was also noted at the 6000 ppm concentration on Days 11-13 and a significant reduction in feed consumption for Days 13-15 was noted at 2000 ppm group. During the exposure period, lacrimation and stained periocular hair, and signs of occular irritation were noted in all groups. Increased incidences of alopecia, lethargy, and salivation were observed in the high-dose dams. No significant differences in pregnancy rate, corpora lutea, fetuses per litter, or the number of stunted fetuses were noted. The mean combined and female fetal weights were significantly reduced in the litters of dams exposed to 12000 ppm. A slight and statistically nonsignificant increase was observed in the incidence of hydrocephalus in the high exposure group.

Test condition: Male and nulliparous female rats were obtained from Charles River Breeding Laboratories, Inc. Females were cohabited with Males (1:1) until copulation was confirmed by the presence of a copulation plug (Day 1 of gestation). A control and three test groups of 24 presumed pregnant female rats were exposed to nominal concentrations of 0, 2000, 6000, and 12000 ppm of the test substance for 6 hours per day on Days 7-16 of gestation. Test atmospheres were generated by vaporization of the test material from glass bottles placed in water baths at 22-26 degree C. The chamber concentrations of t-DCE were determined at approximately 30-min intervals by gas chromatography. During exposures, chamber temperatures, relative humidity, and oxygen concentrations were measured.

Clinical signs were observed twice daily before and after exposures; during the pre- and postexposure periods observations were made each morning. Body weights were recorded on Days 1, 7-17, and 22 and feed consumption was measured on alternate days from 1-19 and on Day 22. At Day 22, dams were killed and the liver and gravid uterus were removed and weighed. Gross pathology was conducted on all dams. The uterus was observed for the types of nidations(live and dead fetuses and resorptions). Live fetuses were weighed, sexed, and examined for external alterations. One half of the fetuses in each litter were examined for visceral alterations. The remaining fetuses were examined for skeletal alterations.

Test substance: The test substance (Trans-1,2-Dichloroethylene) with a purity of 99.64% was provided by PPG Industries, Inc.

Conclusion: Overt maternal and fetal toxicity were demonstrated at concentrations of 6000 ppm or greater and 12000 ppm, respectively. At 2000 ppm, a marginal maternal effect, evident as a significant decrease in feed consumption was found only during Days 13-15 of gestation. This change, however, was not accompanied by a significant decrease in body weight, and, therefore, its biological significance is questionable. Assuming the decrease in feed consumption at 2000 ppm to be a biologically significant change, the NOEL was somewhat less than 2000 ppm for the dam and was 6000 ppm for the conceptus. This result indicated that the test substance is not toxic to the rat conceptus.

Reliability: (1) valid without restriction

26-SEP-2003 (14)

5.8.3 Toxicity to Reproduction, Other Studies

Type: other
In Vitro/in vivo: In vivo
Species: rat
Strain: Sprague-Dawley **Sex:** male/female
Route of administration: inhalation
Exposure period: 90 days
Frequency of treatment: 6 hours/day, 5 days/week
Duration of test: 90 days exposure period and one month recovery period
Doses: 0, 200, 1000, or 4000 ppm
Control Group: yes
Result: No adverse compound-related effects at any concentration levels

Method: other
Year: 1998
GLP: yes
Test substance: other TS

Method: OECD Guideline 413 "Subchronic Inhalation Toxicity: 90-day Study"

Result: The mean analytically determined concentrations of test substance were as targeted: 200, 1000, and 4000 ppm with

standard errors of 0.48, 1.3, and 4.7, respectively. There were no adverse compound-related effects at any concentration level on organ weights and gross and microscopic examination on reproductive organs. The no observed effect level for reproductive effects was 4000 ppm, the highest concentration tested in both male and female rats for this study.

Test condition: Four groups of 15 male and 15 female rats each were exposed to analytically determined mean concentrations of 0, 200, 1000, or 4000 ppm. Rats were exposed whole-body for 6 hours/day, 5 days/week over a 90-day period. Atmospheres containing test substance were generated by metering liquid material into a heated glass flask with either a pump or a syringe drive. The atmospheric concentration of test substance was determined by gas chromatography at approximately 15-minute intervals during each exposure.

Gross pathologic evaluations were performed on 10 males and 10 females/group after approximately 90 days and on 5 males and 5 females/group after a 1-month recovery period. The testes and ovaries were weighed at necropsy. At the end of exposure period, female mammary gland, ovaries, uterus, vagina, prostate, semi vesicles, testes, and epididymides were examined microscopically on 10 males or 10 females from all exposure groups.

Since no treatment-related lesions were found in the high exposure groups, tissues from rats in the recovery group were not examined microscopically.

Test substance: The test substance (Trans-1,2-Dichloroethylene) was supplied by PPG Industries, Inc. as a colorless liquid with a reported purity of 99.86%. The purity of the test substance was confirmed at the laboratory.

Reliability: (1) valid without restriction

26-SEP-2003 (11)

Type: other
In Vitro/in vivo: In vivo
Species: rat
Strain: Fischer 344 **Sex:** male/female
Route of administration: oral feed
Exposure period: 14 weeks
Frequency of treatment: microencapsulated in feed
Duration of test: 14 weeks
Doses: 0, 3125, 6250, 12500, or 50000 ppm
Control Group: yes, concurrent no treatment
Result: No gross or microscopic lesions on reproductive organs were observed.

Method: other
Year: 2002
GLP: yes
Test substance: other TS

Method: The guideline followed for this study was not noted. However, all parameters listed in the OECD/EPA gruidelines for a subchronic toxicity study were evaluated in this study.
Result: Exposure concentrations of 3150, 6250, 12500, 25000, and 50000 ppm in the diet resulted in average daily doses of 190, 380, 770, 1540, and 3210 mg/kg for males and 190, 395, 780, 1580, and 3245 mg/kg for females. Sperm motility and vaginal cytology parameters of exposed rats were generally similar to those of the vehicle controls. There were no treatment-related gross or microscopic lesions on any reproductive organs evaluated for this study.
Test condition: Groups of 10 male and 10 female rats were fed diets containing 3125, 6250, 12500, 25000 or 50000 ppm microcapsulated test substance for 14 weeks. Additional groups of 10 male and 10 female rats received untreated feed or feed containing placebo microcapsules for 14 weeks. Microencapsulation was performed by the analytical chemistry laboratory, Midwest Research Institute and the chemical load was determined to be 45%. The dose formulations were prepared at least every 2 weeks by mixing microencapsulated test substance with feed. At the end of study, sperm count and motility and vaginal cytology evaluations were conducted on rats in the two control groups and the 12500, 25000, and 50000 ppm groups. Necropsies were performed on all core study animals. The right and left testes and left epididymis were weighed. Histopathologic examination on mammary gland, ovary, prostate gland, testis with epididymis and seminal vesicle, and uterus were performed on rats in the untreated control, vehicle control, and 50000 ppm groups.
Test substance: The test substance (Trans-1,2-Dichloroethylene) was obtained from Aldrich Chemical Company, Inc (Milwaukee, WI) in one lot (MP-0224LP). The study laboratory confirmed that the purity was 99% or greater.
Reliability: (1) valid without restriction
09-SEP-2003 (3)

Type: other
In Vitro/in vivo: In vivo
Species: mouse
Strain: B6C3F1 **Sex:** male/female
Route of administration: oral feed
Exposure period: 14 weeks
Frequency of treatment: continual ingestion - microencapsulation
Duration of test: 14 weeks
Doses: 3125, 6250, 12500, 25000, or 50000 ppm
Control Group: yes, concurrent vehicle
Result: No adverse effects on reproductive organs were observed in any exposure groups.

Method: other
Year: 2002
GLP: yes
Test substance: other TS

Method: The guideline followed for this study was not noted. However, all parameters listed in the OECD/EPA gruidelines for a subchronic toxicity study were evaluated in this study.
Result: Exposure concentrations of 3150, 6250, 12500, 25000, and 50000 ppm in the diet resulted in average daily doses of 480, 920, 1900, 3850, and 8065 mg/kg for males and 450, 915, 1830, 3760, and 7925 mg/kg for females. Sperm motility and vaginal cytology parameters of exposed mice were generally similar to those of the vehicle controls. There were no treatment-related gross or microscopic lesions on any reproductive organs evaluated for this study.
Test condition: Groups of 10 male and 10 female mice were fed diets containing 3125, 6250, 12500, 25000 or 50000 ppm microcapsulated test substance for 14 weeks. Additional groups of 10 male and 10 female mice received untreated feed or feed containing placebo microcapsules for 14 weeks. Microencapsulation was performed by the analytical chemistry laboratory, Midwest Research Institute and the chemical load was determined to be 45%. The dose formulation were prepared at least every 2 weeks by mixing microencapsulated test substance with feed. At the end of study, sperm count and motility and vaginal cytology evaluations were conducted on mice in the two control groups and the 12500, 25000, and 50000 groups. Necropsies were performed on all animals. The right and left testes, and left epididymis were weighed. Histopathologic examination on mammary gland, ovary, prostate gland, testis with epididymis and seminal vesicle, and uterus were performed on mice in the untreated control, vehicle control, and 50000 ppm groups.
Test substance: The test substance (Trans-1,2-Dichloroethylene) was obtained from Aldrich Chemical Company, Inc (Milwaukee, WI) in one lot (MP-0224LP). The study laboratory confirmed that the purity was 99% or greater.
Reliability: (1) valid without restriction
09-SEP-2003 (3)

Type: other
In Vitro/in vivo: In vivo
Species: rat
Strain: Sprague-Dawley **Sex:** male/female
Route of administration: drinking water
Exposure period: 90 days
Frequency of treatment: Continuous
Duration of test: 90 days
Doses: 500, 1500, and 3000 mg/kg
Control Group: yes, concurrent no treatment
Result: No adverse effects were observed for organ weight and gross and microscopic evaluations on ovaries and testes.

Method: other
Year: 1987
GLP: no data
Test substance: other TS

Method: The guideline followed for this study was not noted.
Result: Exposure for 90 days to theoretical daily doses of 500, 1500, or 3000 mg/kg/day in drinking water failed to elicit significant compound-related and dose-dependent adverse effects on organ weight measurements and gross and microscopic evaluations of testes and ovaries.

The actual daily doses were 402, 1314, and 3114 mg/kg for males and 353, 1257, and 2809 mg/kg for females.
Test condition: Trans-1,2-dichloroethylene was administered in drinking water solution to five groups consisting of 20 male and 20 female rats. The groups were naive untreated control, 1% emulphor vehicle control, 500 mg/kg, 1500 mg/kg, and 3000 mg/kg. Water solutions were prepared twice weekly by the addition of test substance to 1% emulphor (GAF Corp., Linden, NJ) in deionized water.

At the end of exposure period, an organ weight measurement and gross pathological examinations were performed on testes and ovaries. Testes and ovaries were also examined histologically.
Test substance: The test substance (Trans-1,2-Dichloroethylene) was obtained from Aldrich Chemical Company (Milwaukee, WI). The reported purity was 98%. Identity was confirmed by GC-MS.
Reliability: (1) valid without restriction
26-SEP-2003 (9)

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